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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/716,169	12/17/1996	STEPHEN M. ANDERTON	961125	5487

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	08/716,169	ANDERTON ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-26 and 28-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claim 27 has been canceled.

Claims 24-26 and 28-32 are being acted upon.

2. Applicant's amendment and remarks, filed 9/16/06, are acknowledged. In view of Applicant's amendment and remarks, the previous rejection under 35 U.S.C. 103(a) has been withdrawn. In particular, the reference does not teach the use of the peptide fragments of the instant claims.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 24-25, 29-32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As set forth previously, Applicant has no written description for the use of any peptide derived from a microbial (now mycobacterial) peptide having a conserved mammalian stress homologue. The breadth of the claim reads upon any microbial peptide from bacteria, protozoans and eukaryotic parasites. It is not even clear if science has isolated all the species of bacteria, protozoa and eukaryotic parasites, let alone determine their protein makeup. Furthermore, the only proteins Applicant has described as having peptides meeting the criteria of the claims are hsp65 and glyceraldehydes 3 phosphate dehydrogenase. They have discussed additional potential proteins for use, however no description of the conserved peptides has been disclosed. As such applicant has not adequately described a representative number of species to describe the claimed genus.

Applicant has not offered any new argument in response to this rejection.

5. Claims 24-26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for nasal or oral administration of hsp65 peptides to treat Th1 mediated diseases,

does not reasonably provide enablement for any other route of administration of peptides derived from any other microbial peptides to treat any inflammatory condition.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As set forth in the Office action of 12/04/01, Applicant has not enabled the recitation of the terms "peptides comprising at least 5 amino acids which are identical with corresponding amino acids in the same relative position in a T cell epitope of said mammalian stress protein". The breadth of Applicant's claims would encompass limitless amounts of possible peptides. Applicant has not demonstrated that any peptides out of this entire genus meets the limitations of their claims. The state of the art as taught by Karin et al., demonstrates that a substitution of an phenylalanine with alanine (i.e. a conservative amino acid substitution) at position 89 resulted in an increase in T cell proliferation, binding affinity of the peptide and induction of EAE in rats (a animal model of multiple sclerosis), while the same amino acid substitution, an phenylalanine for an alanine, at position 90, resulted in the exact opposite results, decreased binding, T cell proliferation and no induction of EAE (see Table I, in particular). What the results of the Karin et al., article indicate is that the effects of amino acid changes on peptide-MHC binding, T cell proliferation, and *in vivo* effects of said peptides is unpredictable. Since Applicant has provided little guidance in their specification as to how one of skill in the art would overcome such unpredictability of the effects amino acid changes have on the peptides, it would require an undue of experimentation to practice Applicant's claimed invention.

As set forth in the Office action of 11/25/02, Anderton et al., one of the Applicant's, newly cited, in reviewing the usefulness of APL therapy in humans concluded against the use of APL's in human autoimmune disorders, even though animal data was very promising, and that such an approach in an outbred human population might aggravate rather than reduce pathology (page 370, 1st paragraph 2nd column). In addition, Wendling et al. of which two of the authors are co-inventors, newly cited, clearly teaches that route of administration, nasal worked while parenteral did not, appears to be critical in treating autoimmune diseases with conserved mycobacterial heat shock proteins. Wendling et al., reasons that the stimulation of IL-10 production for bystander suppression appears to be critical for tolerance induction. It is recently known that nasal administration favors IL-10 production while other routes (parenteral) do not. However, such a fine tuning of administration was not disclosed by the instant Application, but appears critical to the enablement of the claimed invention.

Applicant's arguments filed 9/14/06 have been fully considered but they are not persuasive. Applicant argues that a balanced reading of Wendling et al. would not provide reason to doubt the efficacy of the claimed invention. Further, Applicant argues that the reference has no bearing on the instant claims

as the authors used hsp70 and the method of the instant claims employs unrelated hsp65 peptides.

The reference clearly states that the hsp70 peptides "did not suppress disease" when administered parenterally (Abstract). The reference does not reasonably imply that it is simply a matter of "optimization" to make parenteral administration of the hsp70 peptide prevent AA. Indeed, the reference refers to the "failed protection" of parenterally administered hsp70 peptide (page 2716, column 2) and states that additional experiments are needed to even "clarify the role" of IL-10 and cross-reacting T cells (and therefore the effect of hsp70 on them) in disease mechanism. Thus, this reference clearly teaches that the use of hsp70 for the treatment of AA, much less *all* inflammatory disease (the claimed method) has yet to reach the level of invention.

Regarding Applicant's argument that the method of the instant claims employs unrelated hsp65 peptides, Applicant previously argued that the method of the instant claims functions by the same mechanism as the method of Wendling et al. (see particularly the arguments of 10/24/05, page 5), thus the instant argument that the methods are unrelated is not persuasive.

Finally note the Office action of 2/10/05, Janeway et al., teaches that not all inflammatory diseases are T cell mediated. Since the mode of action of administering a hsp65 protein causes IL-10 production and subsequent down regulation of T cell mediated events, one of skill in the art would not expect the hsp65 administration to be useful in inflammatory condition that are not T cell mediated.
This ground for rejection has not bee adequately addressed.

6. The following are new grounds for rejection necessitated by Applicant's amendment.

7. Claims 24-26 and 28-32 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed,

specifically, a method comprising … administering an effective amount of a peptide of 7-30 amino acids having the sequence of a part of the amino acid sequence of a mycobacterial protein … said part comprising at least 5 amino acids which are identical with the corresponding amino acids … at least 4 consecutive amino acids of said 5 amino acids bind identical with the corresponding mammalian stress protein amino acids (Claim 24).

Note that while bits and pieces of the claim might be found throughout the specification, no support for the specific combination of limitations set forth in the method of Claim 24 has been found. Applicant cites previous Claim 27 in support, however, note that Claim 27 is not an original claim. Additionally, Claim 27 previously depended from Claim 26, thus creating a different combination of limitations, i.e., the peptide fragments were from *M. tuberculosis* only and not from any mycobacterial protein as is now claimed.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 24-26 and 28-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically, in Claim 24, "aminoacids" is properly "amino acids".

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina

Chan can be reached on (571) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (571) 308-0196.

13. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see www.pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

1/12/07

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